## REMARKS

Claims 1-3, 5-11 and 13-17 are pending in this application and stand rejected. Applicant respectfully requests reconsideration in view of the Remarks herein.

Claims 1-3 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al. (U.S. Patent 4,830,752) in view of Maeda et al. (U.S. Patent 4,109,663). Applicant respectfully traverses this rejection.

Shibata discloses a separation agent useful for separation of various chemical substances, especially optical resolution of optical isomers. The separation agent comprises 1,3-glucan or a derivative thereof and is preferably β-1,3 glucan, e.g. curdlan. α-1,3 glucan is also disclosed and the preferred degree of polymerization of the polysaccharides disclosed is at least 5, preferably at least 10 and does not exceed 500 because of ease of handling, though there is no special upper limit. When the agent is applied to liquid chromatography, the agent can be used in various forms including powder packed in a column, a coating applied to a capillary column, as a capillary to utilize its inside walls, and spun into fiber and a bundle of fibers used as a column. There is no further description in Shibata of fibers, including any mention of tensile strength, and more importantly no enablement, especially of the criticality of spinning from a liquid crystalline solution having sufficient solids content. All of the Examples in Shibata deal with a 1,3-glucan powder supported on a silica carrier. To Applicant's knowledge there was no method known in the art for preparing a fiber comprising a polymer comprising hexose units wherein at least 50% of the hexose units are linked via an α(1-3) glycoside linkage, said polymer having a number average degree of polymerization of at least 100, and wherein said fiber has a tensile strength of at least 1 gram per denier, prior to his invention. Therefore, Shibata could not have relied on a method of spinning a fiber from an α(1,3) glucan as being well-known in the art.

Maeda et al. is concerned with a smoking tobacco product produced by incorporating in the smoking material a thermo-gelable β-1,3 glucan-type polysaccharide for improved smoking characteristics such as flavor, taste and irritability, and for improved physical properties such as thickness, wet-proof qualities, tensile strength, elongation and filling capacity. The Examiner states that Maeda shows 1,3-glucan fibers having a tensile strength as claimed by Applicant. Applicant respectfully disagrees.

Applicant asserts that Maeda is not relevant prior art to Applicant's invention because Maeda is directed to products made with β(1→3) glucan, not α(1→3). Although both polymers originate from hexose, the two are not the same polymer. Attached hereto are pages from the textbook Principles of Biochemistry, 2nd ed, Lehniger et al., Worth Publishers, 1997 which provide a graphical depiction of the difference between α and β glucan polymers. Although the structures shown refer to the difference between α(1→4) and β(1→4) linkages,

they are pertinent to α(1→3) and β(1→3) linkages. The carbons are numbered in the drawings and the difference between 1-3 and 1-4 bonding in each configuration can be easily construed.

As is shown, polymers having β linkage are structurally different from polymers having α linkage. The enchainment pattern and conformation at the glycoside linkage dramatically affect/determine polymer chain conformation, and therefore such polymers have different physical properties. This is confirmed in Lehninger, *op cit.*, on page 310. As is well known by those of skill in the art, the α(1→4) glucan, amylose, and the β(1→4) glucan, cellulose, are as different as night and day in their physical properties. Chemical properties can also differ, as described in Lehninger, *op cit.* on page 311, e.g. certain enzymes hydrolyze α linkages but not β linkages.

Therefore, Applicant maintains that there is no basis in the art for applying the teachings of Maeda which are limited to β(1→3) glucan polymers to the instant invention which claims fibers comprising a polymer comprising hexose units wherein at least 50% of the hexose units are linked via an α(1→3) glycoside linkage and wherein the fiber has a tensile strength of at least 1 gram per denier.

The Examiner further cites Maeda's Example 6 as teaching a sheet having a thickness of 0.102 mm of the β(1→3) glucan polymer having a tensile strength of 181-220 g/mm. Applicant believes the Examiner has misread Example 6. Applicant respectfully directs Examiner's attention to the wording of Example 6. As stated in Example 6 of Maeda (col 9, lines 31-32): "The tobacco sheets prepared by the procedure set forth in Experiment 5 were measured for...". Thus, in order to know the composition of the sheet measured in Experiment 6, one must refer to Example 5 since in Example 6 no sheet is made, only measured. In Example 5 of Maeda is stated (col 8, lines 55-66): "70 g. of the blended tobacco powder was mixed with the powdered stem (winnower debris), followed by the addition of 10% (on a dry basis) of the pulp fiber as a reinforcement. After thorough drying, 5% each of sucrose and propylene glycol were added. Following the addition of 8% of polysaccharide B, sufficient water was added to the mixture so that the water content of the mixture was 40%. The resulting wet powder was thoroughly homogenized and formed into a web on a press roll plant for tobacco sheet. The web was dried at 100°C to obtain a reconstituted tobacco sheet with a moisture content of about 12%."

It is clear from the description in Maeda that the polysaccharide of Maeda – the β(1→3) glucan – is a minor component (8%) of a sheet and that the other constituents are not polysaccharides. Therefore, the tensile strength of the sheet so formed is not a tensile strength that can be attributed solely to the β(1→3) glucan, as stated by the Examiner. There is no known method in the art for determining the contribution of the β(1→3) glucan to the strength of the total composite sheet. Furthermore, there is no suggestion that the 8% of β(1→3) added to the sheet is in fiber form.

The Examiner states that the tensile strength of the sheet so formed of 181-220 g/mm is within the claimed range. Applicant respectfully requests the Examiner to provide his method of calculation. Applicant has calculated the tensile strength of the sheet by using appropriate unit conversions and has found a strength of 0.02 grams per denier – well outside the claimed range. The conversion is shown below for the convenience of the Examiner:

> 220 $g/mm^2$ converts to 22 $Kg/cm^2$. To convert these units to grams/denier, multiply by 1.098 x $10^{-3}$ / density. Estimating the fiber density to be within the range of 1-1.5 g/cc yields a strength value for the fibers which is in the range of .016 – .024 grams/denier – well below 1 gram/denier.

Applicant's Claims 1-3 are directed to a fiber having a tensile strength of at least 1 gram/denier, not to an α(1→3) polymer alone, and not to a β(1→3) sheet. The properties which are inherent to a material, such as a polymer, should not be confused with the properties which can be imparted to the material by virtue of manipulating that material, e.g. by subjecting that material to processing. While Applicant has discovered that under certain conditions a polymer comprising hexose units wherein at least 50% of the hexose units are linked via an α(1→3) glycoside linkage can be formed into a fiber having a tensile strength of at least 1 gram per denier, as instantly claimed, it is not true that an α(1→3) glucan fiber prepared by whatever means will be characterized by a tensile strength of 1 gram per denier. Applicant has demonstrated this fact in Example 6 and Comparative Example 1 and thus shows that the tensile strength of a fiber is not inherent in a polymer which is a component therein. It is very well known in the art of fiber science that the tensile strength of a spun fiber of a given polymer will exhibit a wide range of properties depending upon the conditions of spinning.

For the reasons stated above, Applicant respectfully maintains that Claims 1-3 are not taught or suggested by Shibata or Maeda or any combination thereof.

Claims 14-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al. (U.S. Patent 4,830,752). Applicant respectfully traverses this rejection.

Shibata in Synthesis Example 3 dissolves 1.3 g of α(1-3) glucan triacetate in a mixture of 9 ml of dichloromethane, 3 ml of acetic acid, and 4 ml of acetic anhydride to which is added 0.05 ml of 7% perchloric acid as part of a process to obtain a powder which will be mixed with silica gel particles and used to resolve several racemic modifications. No liquid crystalline solution comprising any amount of an α(1→3) glucan polymer is formed. Nor would one of skill in the art look at Synthesis Example 3 for a process of forming a liquid crystalline solution comprising a solvent and a polymer having α(1→3) glycoside linkages wherein the amount of polymer provides a solids content of at least 10% from which a fiber could be spun.

For Applicant to have been successful, the α(1→3) glucan polymer had to have had the capability of forming such a liquid crystalline solution. However, Applicant is claiming a liquid crystalline solution comprising a solvent and an amount sufficient to form liquid crystals of a polymer comprising hexose units wherein at least 50% of the hexose units are linked via an α(1→3) glycoside linkage, and wherein the amount of polymer provides a solids content of at least 10%. Applicant is not claiming the polymer alone. Therefore, Applicant maintains that Claims 14-18 are not suggested by Shibata.

Claims 5-11 and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al. (U.S. Patent 4,830,752) for the reasons set forth on pages 4 and 5 of the Office Action mailed August 22, 2003. Applicant respectfully traverses this rejection.

The Examiner points to the 3rd full paragraph of column 3 wherein Shibata mentions a method whereby the resolving agent is spun into fiber and a bundles of the fibers is used as a column. The Examiner further states that "This latter method shows that the preparation of an α(1,3) glucan fiber using a spinning procedure is well known in the art."

Applicant respectfully disagrees that Shibata's mention of fibers in column 3 "shows that the preparation of α(1,3) glucan fiber using a spinning procedure is well known in the art." To Applicant's knowledge there was no known method of spinning an α(1→3) glucan prior to his invention. Applicant invites the Examiner to provide evidence of such a well known method.

Regarding the saponification process in Synthesis Example 4 of Shibata, this is directed to curdlan triacetate, a β(1→3) glucan, and therefore is not applicable to the present invention.

In view of the above, Applicant respectfully maintains that Claims 5-13 are not suggested by Shibata.

In view of the foregoing, allowance of the above-referenced application is respectfully requested.

Respectfully submitted,

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Dated: August 13, 2004
Attachment

SECOND EDITION

# Principles of Biochemistry

## with an Extended Discussion of Oxygen-Binding Proteins

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Late University Professor of Medical Sciences
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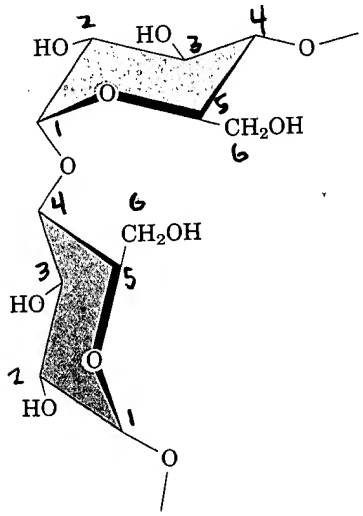
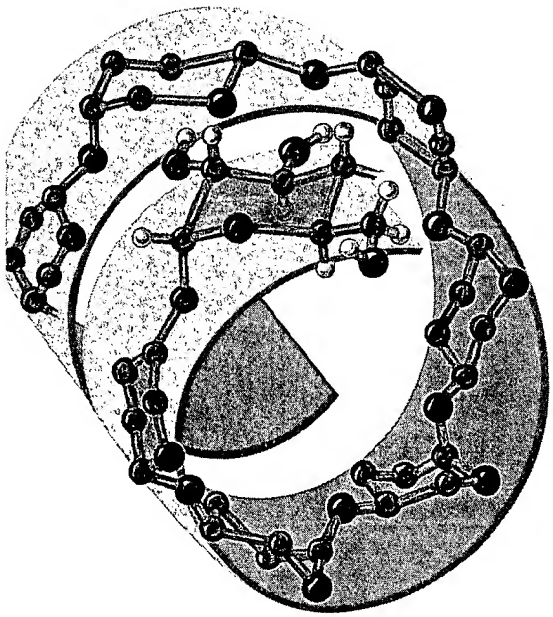



(α1→4)-linked D-glucose units

**(a)**



**(b)**

**Figure 11–16** The structure of starch (amylose). **(a)** In the most stable conformation of adjacent rigid chairs, the polysaccharide chain is curved, rather than linear as in cellulose (see Fig. 11–17). **(b)** Scale drawing of a segment of amylose. The (α1→4) linkages of amylose, amylopectin, and glycogen cause these polymers to assume a tightly coiled helical structure. This compact structure produces the dense granules of stored starch or glycogen seen in many cells (Fig. 11–14).

**Glycogen** is the main storage polysaccharide of animal cells. Like amylopectin, glycogen is a polymer of (α1→4)-linked subunits of glucose, with (α1→6)-linked branches, but glycogen is more extensively branched (branches occur every 8 to 12 residues) and more compact than starch. Glycogen is especially abundant in the liver, where it may constitute as much as 7% of the wet weight; it is also present in skeletal muscle. In hepatocytes glycogen is found in large granules (Fig. 11–14), which are themselves clusters of smaller granules composed of single, highly branched glycogen molecules with an average molecular weight of several million. Such glycogen granules also contain, in tightly bound form, the enzymes responsible for the synthesis and degradation of glycogen.

Because each branch in starch (Fig. 11–15b) and glycogen ends with a nonreducing sugar (one without a free anomeric carbon), these polymers have as many nonreducing ends as they have branches, but only one reducing end. When starch or glycogen is used as an energy source, glucose units are removed one at a time from the nonreducing ends. Because of the branching of amylopectin and glycogen, degradative enzymes (which act at nonreducing ends) can work simultaneously at many ends, speeding the conversion of the polymer to monosaccharides.

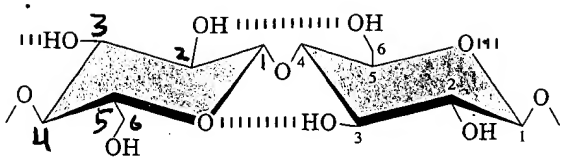
Why not store glucose in its monomeric form? Liver and skeletal muscle contain glycogen equivalent to several percent of their wet weight, in an essentially insoluble form that contributes very little to the osmotic strength of the cytosol. If the cytosol were a 2% glucose solution (about 0.1 M), the osmolarity of the cell would be threateningly elevated. Furthermore, with an intracellular glucose concentration of 0.1 M and an external concentration of about 5 mM (in a mammal), the free-energy change for glucose uptake would be prohibitively large (recall Eqn 10–2).

The three-dimensional structure of starch is shown in Figure 11–16, and is compared with the structure of cellulose below.

## Cellulose and Chitin Are Structural Homopolysaccharides

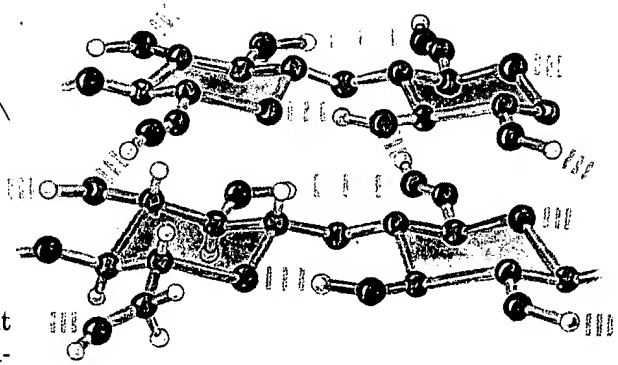
Cellulose, a fibrous, tough, water-insoluble substance, is found in the cell walls of plants, particularly in stalks, stems, trunks, and all the woody portions of plant tissues. Cellulose constitutes much of the mass of wood, and cotton is almost pure cellulose. Because cellulose is a linear, unbranched homopolysaccharide of 10,000 to 15,000 D-glucose units, it resembles amylose and the main chains of glycogen. But there is a very important difference: in cellulose the glucose residues have the β configuration (Fig. 11–17a), whereas in amylose, amylopectin, and glycogen the glucose is in the α configuration. The glucose residues in cellulose are linked by (β1→4) glycosidic bonds. This difference gives cellulose and amylose very different three-dimensional structures and physical properties.

The three-dimensional structure of carbohydrate-containing macromolecules can be understood using the same principles that explain the structure of polypeptides and nucleic acids: subunits with a more-or-less rigid structure dictated by covalent bonds form three-dimensional macromolecular structures that are stabilized by weak interactions. Because polysaccharides have so many hydroxyl groups, hydrogen bonding has an especially important influence on their structures. Polymers of β-D-glucose, such as cellulose, can be represented as a series of rigid pyranose rings in the chair conformation, connected by



(β1→4)-linked D-glucose units

(a)



(b)

**Figure 11–17** The structure of cellulose. **(a)** Part of a cellulose chain; the D-glucose units are in (β1→4) linkage. The rigid chair structures can rotate relative to one another. **(b)** Scale drawing of segments of two parallel cellulose chains, showing the actual conformation of the D-glucose residues and the hydrogen-bond cross-links. In the hexose unit at lower left, all hydrogen atoms are shown; in the other three hexose units all hydrogens attached to carbon have been omitted for clarity, as they do not participate in hydrogen bonding.

an oxygen atom bridging two carbon atoms (the glycosidic bond), about which there is free rotation (Fig. 11–17a). The most stable conformation for the polymer is that in which each chair is turned 180° relative to the preceding subunit, yielding a straight, extended chain. Several chains lying side by side can form the stabilizing network of inter- and intrachain hydrogen bonds shown in Figure 11–17b, resulting in straight, stable supramolecular fibers of great tensile strength. The tensile strength of cellulose has made it a useful substance to civilizations for millenia. Many manufactured products, including paper, cardboard, rayon, insulating tiles, and other packing and building materials, are derived from cellulose.

In contrast to the straight fibers produced by (β1→4)-linked polymers such as cellulose, the most favorable conformation for (α1→4)-linked polymers of D-glucose, such as starch and glycogen, is a tightly coiled helical structure stabilized by hydrogen bonds (Fig. 11–16).

Glycogen and starch ingested in the diet are hydrolyzed by α-amylases, enzymes in saliva and intestinal juice that break (α1→4) glycosidic bonds between glucose units. Cellulose cannot be used by most animals as a source of stored fuel, because the (β1→4) linkages of cellulose are not hydrolyzed by α-amylases. Termites readily digest cellulose (and therefore wood), but only because their intestinal tract harbors a symbiotic microorganism, *Trichonympha,* which secretes cellulase, an enzyme that hydrolyzes (β1→4) linkages between glucose units. Wood-rot fungi and bacteria also produce cellulase. The only vertebrates able to use cellulose as food are cattle and other ruminant animals (sheep, goats, camels, giraffes). The extra stomachs (rumens) of these animals teem with bacteria and protists that secrete cellulase.

Chitin is a linear homopolysaccharide composed of *N*-acetyl-D-glucosamine residues in β linkage (Fig. 11–18). The only chemical difference from cellulose is the replacement of a hydroxyl group at C-2 with an acetylated amino group. Chitin forms extended fibers similar to those of cellulose, and like cellulose is indigestible by vertebrate animals. Chitin is the principal component of the hard exoskeletons of nearly a million species of arthropods—insects, lobsters, and crabs, for example—and is probably the second most abundant polysaccharide, next to cellulose, in nature.

**Figure 11–18** A short segment of chitin, a homopolymer of *N*-acetyl-D-glucosamine units in (β1→4) linkage.